Summary of Safety and Effectiveness

I. GENERAL INFORMATION

Device Generic Name:	Total Hip System, Ceramic Articulation
Device Trade Name:	Novation™ Ceramic Articulation Hip System (AHS)
Applicant's Name and Address:	Exactech, Inc. 2320 N.W. 66th Court, Gainesville, Florida 32653
Premarket Approval (PMA) Number:	P050039
Date of Panel Recommendation:	None
Date of Notice of Approval to the Applicant:	July 5, 2007

The approval of the Novation™ Ceramic AHS is being granted in part due to a licensing agreement with CeramTec AG, who owns the rights to the PMA for the TRANSCEND Ceramic Hip System (P010001) and also manufactures and distributes the ceramic components used in both the Novation™ Ceramic AHS and TRANSCEND Systems. The Novation™ Ceramic AHS uses nearly identical ceramic femoral heads and ceramic acetabular liners (identical articulating geometry) to that of the TRANSCEND System while employing Exactech's own acetabular shells and femoral stems. A component comparison along with preclinical test results were used to demonstrate that the Novation™ Ceramic AHS performs similarly to the TRANSCEND System. Therefore, the clinical data referenced from the PMA for the TRANSCEND System has been used to predict the clinical outcome of the Novation™ Ceramic AHS.

II. INDICATIONS FOR USE

The Novation™ Ceramic AHS is indicated for use in primary total hip arthroplasty in skeletally mature patients with non-inflammatory degenerative joint disease such as osteoarthritis, avascular necrosis, congenital hip dysplasia, and traumatic arthritis.

III. CONTRAINDICATIONS

Use of the Exactech® Novation™ Ceramic AHS is contraindicated in the following situations:

- Active or latent infection in or around the hip joint and other localized infections;
- Acute or chronic systemic infections;
- Skeletally immature patients;

- Neurological or muscular conditions (e.g., prior paralysis, fusion and/or inadequate abductor strength) that could result in instability or overloading of the hip joint;
- Poor skin coverage around the hip joint;
- Patients with inadequate bone stock to allow proper insertion and fixation of the prosthesis;
- Metabolic bone disease and osteoporosis;
- Use in patients with known allergies to the implant materials; and
- Obese patients where obesity is defined as a Body Mass Index (BMI) greater than 35.

IV. WARNINGS and PRECAUTIONS

Please reference the Novation™ Ceramic AHS package insert (Instructions for Use) for the Warnings and Precautions.

V. DEVICE DESCRIPTION

The Novation™ Ceramic AHS is a modular system consisting of a ceramic on ceramic acetabular bearing couple (alumina ceramic femoral head and alumina ceramic acetabular liner) combined with a compatible metal shell (cup) and commercially available screws and Exactech 12/14 titanium alloy and CoCrMo femoral stems identified below. Both the femoral heads and acetabular liner components are manufactured from high-purity dense aluminum oxide ceramic (a.k.a. alumina - Al_2O_3) by CeramTec AG. CeramTec markets this alumina ceramic under the brand name Biolox®*forte*. The alumina conforms to ASTM F603[1] and to ISO 6474[2] material specifications. All implantable devices are supplied sterile (see sterilization section) for single use.

Femoral Heads

The alumina ceramic femoral heads have 12/14 tapers and are offered with outside diameters of 28mm, 32mm and 36mm diameter in three neck lengths (–3.5 mm, +0 mm, +3.5 mm). Exactech® 12/14 Alumina Femoral Heads are only compatible with the Exactech femoral prostheses identified below.

Acetabular Liners (Inserts)

The alumina ceramic acetabular liners are offered in seven sizes with internal diameters of 28mm, 32mm and 36mm. The seven sizes are designated as #140-28-11 (28/37G); #140-32-12 (32/41G); #140-32-13 (32/44G); #140-32-14 (32/48G); #140-36-13 (36/44G); #140-36-14 (36/48G); and #140-36-15 (36/52G). The 28mm ID liner fits shell sizes of 48-50mm OD. The 32mm ID liners fit shell sizes 52-62mm OD. The 36mm ID liners fit shell sizes 54-68mm OD. A male taper-fit connection allows assembly into the mating metal acetabular shell components.

[1] ASTM F603, Standard Specification for High-Purity Dense Aluminum Oxide for Surgical Implant Application
[2] ISO 6474, Implants for Surgery – Ceramic Materials Based on High Purity Alumina

Novation™ Press-Fit Acetabular Shells

The Novation™ Ceramic AHS Acetabular Shells feature a 3-hole cluster design, are hemispherical and offered in 11 sizes with outside diameters ranging from 48 to 68mm in 2mm increments. The titanium alloy (ASTM F-1472[3]) shells are plasma sprayed with a commercially pure titanium coating (ASTM F1580[4]) and are also available with and without a hydroxylapatite coating. The acetabular shells are to be implanted with optional cancellous 6.5mm bone screws (manufactured by Exactech). The shells are designed for uncemented, press-fit use.

Cancellous Bone Screws

The Exactech® 6.5mm cancellous bone screws are optional, require pre-drilling, and are available in two versions, the Exactech® 6.5mm Bone Screw with a full radius tip and the Exactech® MBA 6.5mm Bone Screw with a pointed tip. Both type bone screws are manufactured from titanium alloy (ASTM F136[5]).

Exactech® 12/14 Femoral Stems

The Novation™ Ceramic AHS uses the following commercially available Exactech® cobalt chromium alloy (ASTM F799[6]) and titanium alloy (ASTM F1472) 12/14 femoral stems:

- AcuMatch™ 12/14 P-Series Press-Fit Plasma Femoral Stem
- AcuMatch™ 12/14 L-Series Press-Fit Femoral Stem
- AcuMatch™ 12/14 C-Series Cemented Femoral Stem
- AcuMatch™ 12/14 L-Series Cemented Femoral Stem
- NOVATION™ 12/14 Tapered Press-Fit Plasma Femoral Stem
- NOVATION™ 12/14 Tapered Press-Fit Plasma/HA Femoral Stem
- NOVATION™ 12/14 Splined Press-Fit Plasma Femoral Stem
- NOVATION™ 12/14 Splined Press-Fit Plasma/HA Femoral Stem
- NOVATION™ 12/14 Cemented Femoral Stem

The Exactech® 12/14 femoral stems range in standard and extended offsets. The femoral stems were previously cleared for use in Premarket Notifications K042842, K051335, and K052787.

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[3] ASTM F1472, Standard Specification for Wrought Titanium-6 Aluminum-4 Vanadium Alloy for Surgical Implant Applications

[4] ASTM F1580, Standard Specification for Titanium and Titanium-6 Aluminum-4 Vanadium Alloy Powders for Coatings of Surgical Implants

[5] ASTM F136, Standard Specification for Wrought Titanium-6 Aluminum-4 Vanadium ELI (Extra Low Interstitial) Alloy for Surgical Implant Applications

[6] ASTM F799, Standard Specification for Cobalt-28 Chromium-6 Molybdenum Alloy Forgings for Surgical Implants

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Depending on individual circumstances, alternative procedures may include the use of other commercially available total hip replacement implants, non-surgical treatment such as reduced activity and/or pain medication, or other surgical treatments that do not involve the use of an implant, such as hip joint fusion. Other bearing surface alternatives used in total hip replacement include: ceramic on polyethylene, metal on metal, and metal on polyethylene bearing articulations.

VII. MARKETING HISTORY

The Novation™ Ceramic AHS has not been previously marketed.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The Novation™ Ceramic AHS is similar to the previously approved TRANSCEND Ceramic Hip System (P010001). Exactech references the clinical data from P010001, under a licensing agreement, as clinical support for the Novation™ Ceramic AHS. The clinical data are relevant because the ceramic femoral heads and acetabular inserts of the Novation™ Ceramic AHS have identical articulating surfaces to the ceramic femoral heads and acetabular inserts of the TRANSCEND Ceramic Hip System. A system comparison between the Novation™ Ceramic AHS and the Ceramic TRANSCEND Ceramic Hip System was performed to demonstrate that the systems perform similarly enough on the bench that the clinical data referenced can be used to predict the clinical outcomes for the Novation™ Ceramic AHS.

Please refer to Table 3, Reported Adverse Events, in Section X (Summary of Clinical Investigations) for a tabulation of reported adverse events that occurred in the referenced study (P010001).

List of Potential Adverse Events Associated with Any Total Hip Arthroplasty

- Excessive wear of the implant components secondary to impingement of components or damage of articular surfaces.
- Osteolysis
- Fracture, migration, loosening, subluxation, or dislocation of the prosthesis or any of its components, any of which may require a second surgical intervention or revision.
- Possible detachment of the coating(s) on the femoral stem or acetabular shell components, potentially leading to increased debris particles.
- Unintended bone fractures, including femoral or acetabular perforation while seating the device.
- Metal sensitivity reactions or other allergic/histological reactions to implant materials.
- Superficial or deep infection.
- Delayed wound healing.
- Vascular damage resulting in blood loss and/or hematoma, potentially requiring transfusion.

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- Neurologic injury or neuropathy resulting in transient or permanent weakness, pain, and/or numbness.
- Undesirable leg lengthening or shortening.
- Periarticular calcification or ossification, with or without impediment to joint mobility.
- Cardiovascular disorders including venous thrombosis, pulmonary embolism, or myocardial infarction.
- Gastrointestinal complications.
- Genitourinary complications.
- Aggravation of other joint or back conditions due to positioning during surgery or neurological injury.
- Traumatic arthrosis of the hip from intraoperative positioning of the extremity
- Decreased range of motion.
- Intractable pain.
- Death.

List of Potential Complications Associated with the NOVATION™ Ceramic AHS

In addition to the adverse effects identified above, additional adverse effects may be associated with the NOVATION™ Ceramic AHS as follows:

- Wear of the ceramic acetabular components has been reported following total hip replacement. Higher rates of wear may be initiated by particles of cement, metal, or other debris that can cause abrasion of the articulating surfaces. Higher rates of wear may shorten the useful life of the prosthesis, and lead to early revision surgery to replace the worn prosthetic components;
- While rare, fatigue fracture of the prosthetic component can occur as a result of trauma, strenuous activity, improper alignment, or duration of service;
- Component dissociation; or
- Breakage of the femoral head or acetabular insert.

IX. SUMMARY OF PRECLINICAL STUDIES

The results of the preclinical testing listed below demonstrate that the NOVATION™ Ceramic AHS performs similarly on the bench to the TRANSCEND Ceramic Hip System (P010001). The NOVATION™ Ceramic AHS uses ceramic femoral heads and acetabular liners which have identical articulating geometries to those of the TRANSCEND Ceramic Hip System. In addition, the shell/liner taper locking mechanisms are identical for the two systems. The NOVATION™ Ceramic AHS uses Exactech's own metal acetabular shells and femoral stems to comprise the system. The comparability of the NOVATION™ Ceramic AHS and the TRANSCEND Ceramic Hip System was demonstrated through a side-by-side component comparison and a comparison of preclinical test results.

A battery of preclinical laboratory tests were conducted on the alumina ceramic material used to make the ceramic components. It conforms to the ASTM F603 and ISO 6474 requirements and has been shown to be safe and effective. The metal components that comprise the rest of this system are made from materials that have been used for many years in total hip replacement (THR) surgery.

Preclinical laboratory studies were conducted in support of the design of the NOVATION™ Ceramic AHS. The worst case conditions were established for each component for testing purposes and evaluation as discussed below.

Ceramic Femoral Head Testing

Testing of the ceramic femoral heads was conducted in accordance with the January 10, 1995, FDA *Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems* (FDA Guidance available at http://www.fda.gov/cdrh/ode/355.pdf) at a contact manufacturer. The identified acceptance criteria in each test below are identical to the criteria used to qualify the ceramic femoral heads of the TRANSCEND Ceramic Hip System.

Ceramic Head Static Burst Testing

Static burst or 'crush' testing was performed to evaluate the ability of the individual ceramic head components and the system as a whole to withstand static axial compression. Static burst testing of Biolox *forte* ceramic ball heads used for the NOVATION™ Ceramic AHS was conducted according to the method of ISO 7206-10.[7] Seven tests were performed using 28-12/14L Biolox forte ceramic ball heads on forged CoCr trunnions from Exactech stems representing the worst case combination. Cross-head speed was 2 mm/min. The results showed that the average load to fracture for the heads was 45.3 kN, with no head fracturing below 34.6 kN. The Ceramic Ball guidance document suggests a minimum average burst strength of 46kN with no individual failure below 20N. A t-test was performed comparing the average burst strength value with the mean of a hypothetical burst test sample described by the following statistics: mean = 46.0kN; s.d. =0.0kN, n=7. The t-test yielded a p-value of 0.787, indicating that there was not a statically significant difference between the means of the two samples at the 95% confidence interval. FDA determined that there was not a significant safety concern.

Ceramic Head Fatigue Testing

Fatigue testing of three 28-12/14L Biolox *forte* ceramic ball heads on forged CoCr trunnions was conducted. The applied load was cycled from 14.0 to 0.5 kN at a frequency of 10 Hz in Ringers solution at ambient temperature. All specimens reached 10 million cycles without failure or formation of macroscopically detectable defects, meeting the requirements suggested by the Ceramic Ball guidance.

Post-Fatigue Burst Testing

Following fatigue testing, burst testing of the three samples was performed, with a resulting average burst test value of 27.47 kN and a minimum value of 25.01 kN. These values exceed the 20 kN requirement for the post-fatigue burst strength suggested by the Ceramic Ball guidance.

[7] ISO 7206-10, Implants for surgery – Partial and total hip joint prostheses – Part 10: Requirements, classification and designation of dimensions of bores and cones for prostheses with a modular head

Ceramic Head Pull-off Testing

Five 28-12/14L Biolox *forte* ceramic ball heads were tested for pull-off loads using forged CoCr trunnion, testing at a cross-head speed of 1mm/min. The acceptance criterion was defined as > 250 N. The average pull-off load was 1537 N, and the minimum was 1424 N. These values exceed the sponsor's established acceptance criterion.

The ceramic head testing results indicate that the ceramic heads possess sufficient strength to perform as intended under expected *in vivo* loading conditions.

Ceramic Liner Testing

The NOVATION™ Ceramic AHS Ceramic Liner qualification testing was performed by CeramTec AG. Acetabular shell/liner testing was conducted per the "CeramTec Qualification Program for Ceramic Inserts." The identified acceptance criteria in each test below are identical to the criteria used to qualify the same components of the TRANSCEND Ceramic Hip System. The CeramTec qualification program and acceptance criteria were based on the January 10, 1995, *Guidance Document for the Preparation of Premarket Notifications for Ceramic Ball Hip Systems*; the historical May1, 1995, *Guidance document for Testing Acetabular cup Prostheses*; and data reported by Greenwald et al. and Tradonsky et al.[8,9]

Ceramic Liner Burst Test

The purpose of this test was to determine the minimum burst strength (static axial compression fracture load) for the smallest ceramic liners. Seven worst case 28/37G ceramic liner/48mm acetabular metal shell assemblies were static burst tested using Biolox delta (zirconia composite) ceramic heads. The 28/37G liner/48mm metal shell assembly was determined to be the worst case for all the testing because it has the smallest contact area to distribute applied forces (to resist static compressive loads) within the implant system under consideration.

The acceptance criterion was defined as an average burst strength greater than 46kN with no single sample below 25kN per the CeramTec qualification procedure. The minimum burst value requirement as stated in the Ceramic Ball guidance document was increased to 25kN for ceramic liners to provide an additional factor of safety.

The mean static axial compressive fracture load for the Novation ceramic insert was 74kN with no values below 64kN. This result exceeds the acceptance criteria by a factor of 1.6. The ceramic liner burst testing demonstrates that the liners possess adequate strength to perform as they are intended under expected *in vivo* loading conditions.

[8] Greenwald, A. Seth, S. Tradonsky, P. D. Postak, A.I. Froimson. "Performance Characteristics of Two Piece Acetabular Cups." AAOS 1991, 10M0591.

[9] Tradonsky, S., P.D. Postak, A.I. Froimson, A.S. Greenwald. "A Comparison of the Dissociation Strength of Modular Acetabular Components." Clinical Orthopaedics and Related Research 1993; 296: 154-60.

Ceramic Liner Fatigue/Post-Fatigue Burst Test

The purpose of this test was to determine the minimum burst strength for the worst case liner assembly after cyclic fatigue testing. Three worst case 28/37G ceramic liner/48mm acetabular metal shell assemblies were fatigue tested in axial compression using an applied load cycled from 14.0 kN (3150 lbs) to 0.5 kN at a frequency of 10 Hz in Ringers solution at ambient temperature for 20 million cycles. No failures or fractures occurred.

The acceptance criteria required the ceramic liner samples to pass 20 million cycles at 14kN with no macroscopically visible component failure and have no post-fatigue burst strength below 25kN per the CeramTec qualification procedure.

Fatigued alumina liners were then burst tested using systems comprised of the alumina ceramic inserts and Biolox delta (zirconia composite) ceramic heads. The mean post-fatigue burst strength for the Novation ceramic insert was 59kN with no values below 58kN. This result exceeds the acceptance criterion by a factor of 2.4 and the 20kN value suggested for ceramic femoral heads in the FDA Ceramic Ball guidance document (no requirements currently exist for ceramic liners). The ceramic liner testing demonstrates that the liners possess adequate strength to perform as they are intended under expected *in vivo* loading conditions.

Ceramic Liner Push-out Testing - Pre-fatigue and Post-fatigue

The purpose of this pre-fatigue and post-fatigue push-out testing was to evaluate the integrity of the liner/shell connection (i.e. locking mechanism) of the acetabular system. Five worst case 28/37G ceramic liner/48mm acetabular metal shell assemblies underwent pre-fatigue push-out force testing. The 28/37G liner/48mm metal shell assembly was determined to be the worst case for all of the testing because it represents the thinnest insert available in the 28mm diameter size, which is the worst case with respect to push-out resistance and has least amount of taper surface contact area.

The acceptance criterion required an average push-out value greater than 200N per the CeramTec qualification procedure. The mean pre-fatigue push-out force was 859N with no values below 688N. The subject pre-fatigue push-out strength is 4.3 times greater than the 200N criterion value.

Post-fatigue push-out testing was also conducted. Five worst case 28/37G ceramic liner/48 mm acetabular metal shells were fatigued via 14kN load for 5 million cycles with no failures or fractures. The mean post-fatigue push-out force was 9460N with no values below 7130N. The post-fatigue push-out force is 10 times greater than the force of the initial push-out test and 47.3 times greater than the acceptance criteria of 200N. The increase in the post fatigue push-out testing indicated that the locking taper interlock is enhanced after cyclic loading. The integrity, therefore, of the ceramic liner/shell connection i.e. locking mechanism of the acetabular system as tested in pre-fatigue and post-fatigue push-out demonstrates that the ceramic/metal shell construct locking mechanism exceeds the 200N acceptance criterion and should perform as intended under expected *in vivo* loading conditions.

Acetabular Liner Rotational Stability (Torsional Test)

The purpose of this torsional test was to evaluate the integrity of the liner/shell connection i.e. locking mechanism of the acetabular system by determining the torsional force required to dissociate the taper-fit between a ceramic liner and an acetabular shell. Three worst case 28/37G ceramic liner/48 mm acetabular metal shells underwent torsional testing. The 28/37G liner/48mm metal shell assembly was determined to be the worst case for the testing because it has the least amount of taper surface contact area within the Novation implant system under consideration.

The acceptance criterion was defined as an average torsional force greater than 4N*m (400N*cm) per the CeramTec qualification procedure. This acceptance criterion was based on the fact that the torque due to friction at the ball-liner interface is approximately 2.4N*m and the locking mechanism of the liner in the shell should exceed this by a factor of safety. The defined acceptance criterion exceeds the 2.4N*m acceptance criterion by a safety factor of 1.7.

The mean rotational moment (torque) of the acetabular construct was 1341N*cm with no values below 800 N*cm. This result exceeds the 4N*m acceptance criterion by a factor of 3.35.

The integrity of the ceramic liner/shell connection (i.e. locking mechanism) of the acetabular system as tested in torsion demonstrates that the ceramic/metal shell construct locking mechanism exceeds the 400N*cm acceptance criteria and therefore, should perform as intended under expected *in vivo* loading conditions.

Acetabular Liner Lever-Out Test

The purpose of this test was to evaluate the integrity of the liner/shell connection i.e. locking mechanism of the acetabular system by determining the lever-out force required to dissociate the taper-fit between a ceramic liner and an acetabular shell. Three worst case 28/37G ceramic liner/48 mm acetabular metal shells underwent lever-out testing. The 28/37G liner/48mm metal shell assembly was determined to be the worst case for the testing because it has the least amount of taper surface contact area within the Novation implant system under consideration.

The acceptance criteria was defined as an average lever-out strength greater than 3000N*cm (30N*m) per the CeramTec qualification procedure.

The mean lever-out force of the acetabular construct was 6470N*cm with no values below 4795 N*cm. The integrity of the ceramic liner/shell connection (i.e. locking mechanism) of the acetabular system as tested in lever-out testing demonstrates that the ceramic liner/metal shell construct locking mechanism exceeds the 3000N*cm acceptance criterion by a factor of 2.2 and therefore, should perform as intended under expected *in vivo* loading conditions.

Range of Motion, Head/Liner Constraint

The Novation™ Ceramic AHS is a semi-constrained total hip system in that it limits movement in one or more planes due to the geometry of its articulating surfaces. A computer aided design (CAD) range of motion (ROM) analysis of the total hip construct was performed to measure the constraint in terms of Click-to-Click ROM for a comparison between the Novation™ Ceramic AHS and the TRANSCEND Ceramic Hip System. Click-to-Click motion was defined by the motion of the femoral component from initial contact between the neck at rest on the liner, to placing the neck to rest on the opposite side of the liner. ROM measurements were made for each Exactech femoral stem, femoral head and acetabular cup combination representing worst case scenarios to establish the worst case (minimum) ROM values. The acceptance criterion was defined as ROM $\geq 117°$ based on minimum ROM values for the TRANSCEND Ceramic Hip System. The worst case (least ROM) combination of implants was determined using the 12/14 taper Exactech L-series press Fit Stem (size 6), a 28mm -3.5 ceramic head, the 28/37G ceramic liner and the 48mm acetabular metal shell. The AcuMatch L-Series femoral stem represents the least ROM for all stems offered by Exactech due to the absence of the neck flat geometry common to all other Exactech femoral stems. The worst case combination yielded 119° minimum ROM. All construct combinations exceeded the established acceptance criterion.

Wear of Alumina Ceramic-on-Ceramic Hip Bearings

PMA P010001, incorporated by reference, includes results of a wear test designed to replicate an *in vivo* condition, comparing the amount of wear debris produced by the 28mm ceramic-on-ceramic couple to that of the traditional couple of polyethylene and cobalt chrome. This test is relevant to the Novation™ Ceramic AHS submission because the Novation™ Ceramic AHS has identical articulating geometry of the ceramic on ceramic interfaces as that of the ceramic on ceramic components used in the testing reported in P010001.

The data from P010001 indicated that dimensional changes for the ceramic components after five million cycles were still below the resolution of the coordinate measuring system (2 μm). Weight loss and dimensional changes were too insignificant to be detected. There was a slight increase in surface roughness for both head and liner. The wear results conducted from this test showed that the ceramic on ceramic articulation surfaces used for the Novation™ Ceramic AHS produce no detectable wear after five million cycles.

Ring-on-Disk Test

PMA P010001 includes results of a ring-on-disk test conducted according to ISO standard 6474. This test is also applicable to the Novation™ Ceramic AHS submission because its ceramic components have identical articulating geometries to the ceramic components used in the test. The device was tested for 120 hours and the depth of the wear mark was below 1 μm. According to the results, the specimen met ISO 6474 with respect to wear resistance, allowing an average wear rate of $0.01 mm^3/h$.

Sterilization

Exactech® ceramic femoral heads and ceramic liners are sterilized by gamma radiation sterilization (Cobalt 60 Source). The process is validated and periodically revalidated per the requirements of ANSI/AAMI/ISO 11137:1995, Sterilization of health care products – Requirements for validation and routine control – Radiation sterilization (VD Max dose setting method) to yield a minimum Sterility Assurance Level (SAL) of 10^{-6}.

X. SUMMARY OF CLINICAL TESTING

As previously stated, the Novation™ Ceramic AHS is similar to the previously approved TRANSCEND Ceramic Hip System (P010001). Exactech, Inc. references the clinical data from P010001, under a licensing agreement, as clinical support for the safety and effectiveness of the Novation™ Ceramic AHS. The clinical data are relevant because the two systems use identical ceramic components in terms of material composition and articulating geometry. The Novation™ Ceramic AHS uses Exactech's own acetabular shells (designed to mate with the ceramic liners) and a subset of Exactech's available femoral stems. The two systems were shown to perform similarly in preclinical bench testing.

Published Literature

Published literature on early results of the TRANSCEND Ceramic Hip System discusses significant improvement in average Harris Hip Scores and SF-12 scores when compared to pre-operative scores. No fractures of the ceramic components were reported in these articles.[10,11]

Pivotal Clinical Study

The pivotal clinical study of the TRANSCEND Ceramic Hip System was a prospective, multi-center, non-masked clinical trial of 959 procedures in 848 patients, comparing the referenced ceramic hip system to an historical control group.

Although the primary efficacy endpoint in the clinical study was the survivorship of the referenced ceramic hip system (as assessed at the two year postoperative interval), for the purposes of the clinical study, the primary efficacy endpoints included Harris Hip Score and radiographic assessments at two years as well. In addition, patient satisfaction was assessed by the SF-12 at two years.

Complication rates were the primary safety endpoint.

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[10] Garino, Jonathan P., M.D. "Modern Ceramic-on-Ceramic Total Hip Systems in the United States." *Clinical Orthopaedics and Related Research* 2000; 379:41-47.

[11] Murphy, Stephen B., M.D., and Wael K. Barsoum, M.D. "Ceramic-Ceramic Bearings in Total Hip Arthroplasty: Preliminary Clinical Results." *The Orthopaedic Journal at Harvard Medical School* 2001; 3:92-94.

Study Design

The study was a prospective, multi-center, historical control, clinical trial. The historical control group was later selected as the population implanted with a metal on polyethylene hip consisting of non-inflammatory degenerative joint disease cases. Study patients consisted of individuals over 21 years of age presenting for total hip arthroplasty due to osteoarthritis, congenital hip dysplasia, traumatic arthritis and avascular necrosis. A total of 329 procedures were performed with the referenced ceramic hip system in the original clinical population (Original Clinical Population). An additional 630 procedures were implanted under Continued Access. The total number (Original Clinical Population and Continued Access) meeting the inclusion/exclusion criteria as required by the protocol is 959 procedures in 848 patients. Over a two-year period, 211 hip prostheses (179 patients) with metal femoral stems and plastic cups were implanted in the control group.

Pivotal Clinical Patient Assessment

Each patient was evaluated at the immediate and 6, 12, and 24-month post-operative intervals, unless otherwise indicated by complications. At each follow-up visit, a Harris Hip Score and SF-12 was administered as well as obtaining AP and lateral radiographs. Radiographs were reviewed by the implanting surgeon. There were no pre-specified success/failure criteria in the clinical study.

Demographics

For the study population, there were 965 procedures performed in 854 patients at 12 sites by 19 surgeons. Six of these patients did not meet study inclusion criteria (one procedure enrolled as a revision for a previously implanted hip and five procedures performed in patients with rheumatoid arthritis). These six procedures are excluded from this analysis. Therefore, the primary analysis sample included 959 procedures for first hip replacements performed in 848 patients.

The patient accounting and baseline demographics are summarized in Tables 1 and 2. Note that there were nine deaths, none of which was related to the study or to the device.

Table 1: Patient Accounting

Evaluation Interval	Original Clinical Patient Population (n=329)			Continued Access Population (n=630)		
	TFU	EFU	AFU (%)	TFU	EFU	AFU (%)
Pre-Op	329	329	100% (n=329)	630	630	100% (n=630)
6 months	329	323	93% (n=300)	602	602	71% (n=430)
12 months	329	321	91% (n= 293)	443	442	53% (n=233)
24 months	329	321	94% (n=302)	151	150	0% (n=0)

TFU = Theoretical Follow-Up; EFU = Expected Follow-Up (Theoretical Follow-Up minus deaths and removals without replacement); AFU = Actual Follow-up

Table 2: Baseline and Demographics

Values	Total Study Procedures (n=959)	Historical Control Group (n=211)
Mean Age in years	51.4 years (range 20-80)	62.7 years (range 22-87)
Gender	595 (62%) Males 364 (38%) Females	112 (53%) Males 99 (47%) Females
Mean Body Mass Index (kg/m^2)	28.8 (range 17.7-65.8)	27.1 (range 22.8-40.9)
Diagnosis Osteoarthritis Avascular Necrosis Traumatic Arthritis Congenital Hip Dysplasia	 692 (72.2%) 189 (19.7%) 36 (3.8%) 42 (4.4%)	 180 (85.3%) 31 (14.7%) 0 0
Mean Baseline Total HHS (range 1-100)	45.1 (range 8.3-95.9)	42.7 (range 11-79)
Mean Baseline Pain HHS (range 0-44)	12.9 (range 0-44)	13.2 (range 0-30)
Mean Baseline Harris ROM, degrees (range 0-5)	3.8 (range 3.1-4.88)	4.1 (range not available)

Safety & Effectiveness Data

Safety Results

The adverse events related to total hip replacement surgery reported in the pivotal clinical study of 959 procedures in 848 patients are listed in Table 3.

Table 3: Reported Adverse Events

Event	Ceramic TRANSCEND Clinical Study (n=959)		Historical Control Group (n=211)	
Systemic	**Freq.**	**% of Pop.**	**Freq.**	**% of Pop.**
Deaths	9	0.9%	0	0%
Pulmonary Embolism	2	0.2%	2	0.9%
Deep Vein Thrombosis	4	0.4%	0	0%
Local	**Freq.**	**% of Pop.**	**Freq.**	**% of Pop.**
Revisions/Removals[1]	11	1.1%	8	3.8
Breakage/Fracture of Component[2]	5	0.5%	2	0.9%
Dislocation (single) of Component[3]	8	0.8%	3	1.4%
Dislocation (recurrent) of Component[4]	2	0.2%	0	0%
Femoral Fracture	18	1.9%	9	4.3%
Hematoma	2	0.2%	0	0%
Heterotopic Ossification	1	0.1%	1	0.5%
Infection: Deep, Early < 1year	2	0.2%	0	0%
Infection: Deep, Late >1 year	1	0.1%	0	0%
Infection: Superficial	7	0.7%	0	0%
Loosening of Component	3	0.3%	2	0.9%
Migration of Component	2	0.2%	0	0%
Persistent Foot Drop	2	0.2%	0	0%
Pain	10	1.0%	0	0%
Perforation of Femur During Reaming	2	0.2%	0	0%
Wear of Component	1	0.1%	0	0%
Subsidence of Component	3	0.3%	2	0.9%
Soft Tissue Trauma	0	0%	0	0%
Wound Problems	2	0.2%	0	0%
Other Local Complication[5]	10	1.0%	0	0%
Local - Hip	**Freq.**	**% of Pop.**	**Freq.**	**% of Pop.**
Trochanteric Bursitis	16	1.7%	1	0.5%
Trochanteric Non-union	0	0%	0	0%
Trochanteric Avulsion	4	0.4%	0	0%

Notes:

[1] See details in the following Table 4 for n=959.

[2] Clinical Study : Chipping of ceramic acetabular liner during placement requiring intraoperative revision.
Historical Control Group: Broken metal peg of acetabular cup

[3] 2 were revised for this reason

[4] 1 was revised for this reason.

[5] Consisted of: 3 cases of irritation/inflammation; 2 cases where patients fell; 1 case of component mismatch; 1 case of liner malposition; 1 case where the acetabular shell seated too deeply in the reamed cavity; 1 case of hip flexor weakness; and 1 case where the anterior abductor pulled off. None of these complications were related to the study hip or the procedure.

Revisions and Removals

Eleven devices out of the 959 procedures in the trial have been revised or removed. Table 4 summarizes the clinical information pertaining to these cases.

Table 4: Summary of Revisions and Removals

Procedures	Age/ Gender	Diagnosis	Duration of Implantation	Reason for Revision/Removal
Revision of acetabular component with bone graft and cage implantation	50/F	AVN	84 days	Migration of acetabular component
Revision of femoral head with a longer neck	29/F	Congenital hip dysplasia	1 day	Dislocation
Replaced acetabular component to larger size (32mm) and replaced femoral head to 35mm	43/M	Severe osteoarthritis with mild hip dysplasia	1 day	Dislocation
Replacement of acetabular component, liner, and femoral head. Repair of abductor mechanism.	62/M	Osteoarthritis	38 days	Persistent dislocation following closed reduction; trochanteric fracture with avulsion of abductors
Revision followed by removal and girdlestone procedure	51/M	Traumatic arthritis	210 days	Deep infection and stitch abscess
Replacement of acetabular liner	36/F	Congenital hip dysplasia	3 days	Acetabular liner disassociated from shell
Replacement of acetabular liner and femoral head	41/M	Osteoarthritis	14 days	Increasing pain, suspected infection
Replacement of acetabular liner and femoral head	58/M	Avascular necrosis	953 days	Excessive wear due to impingement on acetabular cup rim
Replacement of femoral head from 32mm to 28mm	50/M	Osteoarthritis	1 day	Liner/head size mismatch noted on postoperative film
Replacement of (uncemented) femoral stem to cemented stem	56/M	Osteoarthritis	657 days	Pain and progressive subsidence due to undersized (uncemented) femoral stem
Replacement of femoral stem and head	56/F	Osteoarthritis	786 days	Femoral component loosening

Efficacy Results

Table 5, below, shows the mean and range of Harris Hip Scores for each study cohort preoperatively and two years postoperatively.

Table 5: Efficacy Results - HHS

Primary Efficacy Assessment	Original Patient Population (n=329)[1]	Continued Access Population (n=630)[2]	Historical Control Group (n=211)
Preoperative mean HHS (range)	44.8 (13-89)	45.2 (8-96)	42.7 (11-79)
2 year postop mean HHS (range)	94.8 (34-100)	88.1 (17-100)	92.7 (39-100)
% Excellent/Good Results (HHS 80-100 points) at 2 years postop	92.2%	76.9%	88.2%

Notes:

[1] Original clinical population includes the first 329 procedures enrolled in the clinical study. This includes replacements and removals prior to 24 months (n=9), deaths prior to 24 months (n=7), and cases in which only a partial Harris Hip Score at 24 months or later was available (n=4)

[2] The *Continued Access* sample (N=630) includes procedures performed after the original clinical population without Month 24+ outcomes. Therefore, outcomes reported were defined on the basis of Last Observation Carried Forward (LOCF) and represent the latest clinical results available for that procedure.

Any Radiographic Lucency

Radiolucencies were recorded at each follow-up visit based on if they involved the entire Gruen zone (seven AP femoral zones, seven lateral femoral zones, three AP acetabular zones, and three lateral acetabular zones). Table 6 summarizes these results.

Table 6: Any Radiolucency

Lucency	Original Study Population (n=329)	Historical Control Group (n=211)
Femoral	18 (5.5%)	66 (31.3%)
Acetabular	9 (2.8%)	56 (26.5%)
Overall	22 (6.8%)	77 (36.5%)

In addition, any subsidence was reported for the original study population for 0.9% of the femoral stems and 0.3% of the acetabular cups. In the historical control group there were two instances of femoral stem subsidence (1.0%).

Implant Survivorship

Implant survivorship was the pre-specified primary endpoint in the pivotal clinical study of the referenced ceramic hip system. Kaplan-Meier cumulative survivorship over time is shown in Tables 7 and 8 for the referenced ceramic hip and the historical control group over time.

The cumulative Kaplan-Meier survivorship values for the femoral or acetabular component are shown in Tables 7 and 8 based on the longest duration of follow-up available in each study cohort.

Table 7: Referenced Ceramic Hip System Implant Survivorship

Interval	Number Entering Interval	Number Withdrawn	Number Revised in Interval	Cumulative Survival	Standard Error
12 months	528	69	8	0.9909	0.0041
24 months	279	78	1	0.9876	0.0066
36 months	1	0	0	0.9308	0.0562

Table 8: Historical Control Group Implant Survivorship

Interval	Number Entering Interval	Number Withdrawn	Number Revised in Interval	Cumulative Survival	Standard Error
12 months	234	8	3	0.9870	0.0074
24 months	223	70	1	0.9817	0.0090
36 months	152	103	1	0.9719	0.0131
48 months	48	34	3	0.8779	0.0481
60 months	11	11	0	0.8779	0.0481

Patient Success Criteria

Table 9 describes the proportion of patients meeting individual clinical success criteria at two years postoperatively.

Table 9: Patient Success Criteria at 2 Years

Patient Success Criteria	Original Patient Population (n=329)[1]		Historical Control Group (n=211)	
Absence of Revision (%)	96.7%	(n=318)	98.1%	(n=207)
Total HHS ≥ 70	96.8%	(n=318)	95.3%	(n=201)
No Complete Radiolucencies[2]	99.7%	(n=328)	88.5%	(n=184)

Notes:

[1] The *Original Patient Population* sample includes procedures in the *Complete Endpoint* (N=309) sample plus procedures with revisions, replacements, or removals prior to Month 24 (N=9); who died prior to Month 24 (N=7); or who had only a partial Harris Hip Score assessment at Month 24 or later (N=4). This sample was constructed in order to facilitate an analysis of efficacy and safety endpoints for hips that were at-risk for a complication and that 'completed the study'. For *Complete Follow-up* procedures (N=329), the Month 24+ endpoint was defined as the Month 24 value and if not available, values after Month 24 were used. Original clinical study population includes the first 329 procedures enrolled in the clinical study. This includes replacements and removals prior to 24 months (n=9), deaths prior to 24 months (n=7), and cases in which only a partial Harris Hip Score at 24 months or later was available (n=4).

[2] Absence of complete radiolucency was determined by radiographic evaluation for four views: acetabular AP view (3 regions), acetabular lateral view (3 regions), femoral stem AP view (7 regions), and femoral stem lateral view (7 regions). Complete radiolucency in a view was defined to be present if there was any radiolucency present in all zones comprising that view. Absence of complete radiolucency was defined to be present if none of these four views had complete radiolucency.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The preclinical and referenced clinical data provide reasonable assurance that the Exactech Novation™ Ceramic AHS is safe and effective for total hip replacement in patients with osteo-degenerative arthritis, avascular necrosis, and related diagnoses.

A system comparison analysis between the Novation™ Ceramic AHS and the TRANSCEND Ceramic Hip System (P010001) demonstrated that the systems perform similarly on the bench and that the clinical data referenced in Section X can be used to predict the clinical outcomes for the Novation™ Ceramic AHS.

XII. PANEL RECOMMENDATIONS

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA application was not referred to the Orthopedic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

The applicant has adequately submitted all answers to the FDA's questions and comments for their PMA application. The preclinical data and similarities in device design to the previously approved ceramic hip system (P010001) provide reasonable assurance that he Novation™ Ceramic AHS is safe and effective when used as directed for primary total hip arthroplasty in skeletally mature individuals with noninflammatory degenerative joint disease such as osteoarthritis, avascular necrosis, congenital hip dysplasia, and traumatic arthritis.

In addition, the applicant has agreed to conduct a 10 year post-approval study to evaluate the long term safety and effectiveness of the Exactech Novation™ Ceramic AHS. The study will enroll a minimum of 250 patients, of which a minimum of 175 patients will be followed out to five years and a minimum of 100 patients will be followed out to 10 years. During the first five years of the study, clinical (HHS, adverse events), radiographic, and patient self-assessment (SF-12) information will be collected for each subject. For the sixth through the tenth postoperative years, patients will be asked to return an outcomes questionnaire designed to determine the survivorship status of their hip replacement.

The applicant's manufacturing facilities were inspected and determined to be in compliance with the Quality System Regulation (21 CFR Part 820).

FDA issued an approval order on July 5, 2007.

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See the Device Labeling

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Post-Approval Requirements and Restrictions: See Approval Order.